# PULMONARY VASCULAR DILUTION CURVES RECORDED BY EXTERNAL DETECTION IN THE DIAGNOSIS OF LEFT-TO-RIGHT SHUNTS

BY

## ROLAND FOLSE AND EUGENE BRAUNWALD

From the Cardiology Branch and the Clinic of Surgery, National Heart Institute, Bethesda, Maryland

Received September 7, 1961

In the past few years præcordial isotope dilution curves have been used with increasing frequency to investigate the central circulation. By such techniques it has been possible to estimate the cardiac output (Veall et al., 1954; Huff et al., 1958; MacIntyre et al., 1958; and others), the fraction of ventricular end-diastolic volume discharged per beat (Cournand et al., 1960; Folse and Braunwald, 1961), the pulmonary transit time (Shipley and Clark, 1956), and "pulmonary" blood volume (Lammerant and de Visscher, 1956), as well as to detect circulatory shunts (Prinzmetal et al, 1949; Huff et al., 1957; Greenspan et al., 1959; Turner et al., 1960; Shapiro and Sharpe, 1960; Cornell et al., 1960 and 1961). The technique which has been found useful in the assessment of left-to-right shunts consists of the intravenous injection of a gamma-emitting radio-isotope and the recording of dilution curves by means of a scintillation detector placed over the præcordium. Since the isotope passing through both sides of the heart is detected by the scintillation crystal, the resultant curve is a complex one, and represents the partial superimposition of two curves, one from each side of the The relative contribution of each ventricle to the recorded curve depends on a number of factors including the relative size of both ventricles, their anatomic positions within the thorax, the precise placement of the detector and its degree of collimation. In the presence of a left-to-right circulatory shunt, this complex curve is also modified by the recirculation of isotope within the central circulation.

In an attempt to simplify the interpretation of præcordial dilution curves the technique has been modified so that the detector was placed over a peripheral lung field. The resultant dilution curves, which resemble those illustrated by Huff et al. (1957), are simpler monophasic curves and represent the time-concentration relationships of the indicator passing through the pulmonary vascular bed beneath the detector. Dollery et al. (1961) have described a technique for the estimation of pulmonary blood flow by determining the clearance rate of inspired radioactive carbon dioxide with radiation counters placed over the chest; this method also appears to be a sensitive one for detecting circulatory shunts. The present report summarizes the technique employed and the clinical experiences with pulmonary vascular isotope dilution curves following intravenous injection of the indicator in 33 patients.

#### **METHODS**

Curves were obtained in 17 patients subsequently shown to have left-to-right circulatory shunts. They ranged in age from 5 to 48 years, the average being 21 years. The presence of the shunt was proven at operation in 9 of these cases, and by means of the inhaled Kr<sup>85</sup> test at right heart catheterization in the other 8 (Braunwald *et al.*, 1961). Of the 17 patients, 4 had patent ductus arteriosus, 7 ventricular septal defects and 6 atrial septal defects.

Sixteen patients without left-to-right circulatory shunts, ranging in age from 7 to 54 years (Av.=26 years), were also studied. Eleven of these had previously undergone operations for closure of a left-to-right shunt, 3 had rheumatic mitral or aortic valve disease with congestive heart failure. In all 16 patients the absence of a left-to-right shunt was proved at catheterization by means of the inhaled Kr<sup>85</sup> test and the recording of arterial indicator dilution curves following intracardiac injection.

The radiation detector employed for these studies was a 3 in. diameter, thallium activated sodium iodide crystal\* surrounded by a collar of lead, one inch in thickness; collimation was provided by a tapered lead shield extending 12.5 cm. beyond the surface of the crystal with an aperture having a diameter of 3.8 cm. The efficiency characteristics of the collimator are illustrated in Fig. 1. The

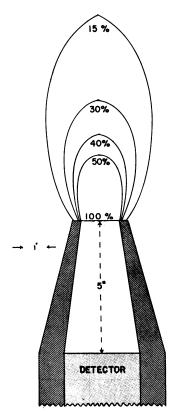


Fig. 1.—Cross-sectional drawing illustrating the position of the detector, the lead shield and the efficiency characteristics of the detector and collimator.

detector field lines represent the percentage radioactivity detected as a point source was moved away from the aperture. The photomultiplier of the scintillation detector was led into a count rate meter, with a response time of 0.5 or 1.0 sec., and the output of the rate meter was led to the D.C. preamplifier of a multichannel oscilloscopic photographic recorder.

All the studies were carried out with patients in the supine position (Fig. 2). The scintillation detector was placed over the right or the left upper lung field, and positioned so that the aperture of the collimator was in contact with the skin, and the long axis of the crystal was perpendicular to the chest wall. The centre of the aperture was adjusted to be over the second intercostal space 1 to 2 cm. lateral to the midclavicular line.

Fifteen to 40 microcuries of  $I^{131}$ -labelled diodrast were injected either into a femoral or an antecubital vein, and rapidly flushed with 10 ml. of saline. The resulting curves were analysed in the following manner. The build-up time  $(T_1)$  was first determined. This was represented by the time interval between the appearance of isotope under the detector and the time of the peak activity. This peak activity  $(C_1)$  was measured, as well as the activity  $(C_2)$  which was present at a time which followed  $C_1$  by an interval equivalent to the build-up time. The ratio of activity  $C_2$  to activity  $C_1$  was then determined and expressed as a percentage (Fig. 3).

#### **RESULTS**

The initial portion of the descending limbs of the dilution curves in patients without left-to-right shunts were smooth and almost as rapid as the ascending limbs. Interruption of the descending limb normally occurred near the bottom of the curve and the level of activity then showed little further decline to the new background level (Fig. 3). In the patients with

congestive heart failure both the ascending and descending limbs of the curves were symmetrically prolonged (Fig. 4).  $C_2/C_1$  ranged from 21 per cent to 41 per cent and averaged 31 per cent in the 16 patients without circulatory shunts (Fig. 5).

In the patients with left-to-right circulatory shunts the ascending limbs were rapid and had appearances similar to those observed in the patients without shunts; however, the descending limbs declined slowly and reached the new background level much more slowly (Fig. 6-8). In these patients  $C_2/C_1$  ranged from 46 per cent to 94 per cent and averaged 66 per cent (Fig. 5).

<sup>\*</sup> Model PS5R-1, Nuclear-Chicago Corporation.

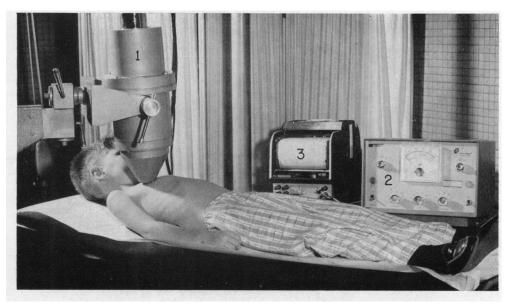


Fig. 2.—Photograph of the experimental arrangement employed. 1=shield surrounding detector. 2=count rate meter. 3=recorder.

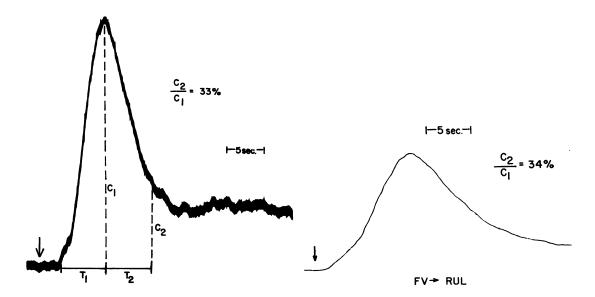


Fig. 3.—Pulmonary vascular dilution curve in a patient with a normal circulation.  $T_1$ =build-up time,  $C_1$ =peak concentration. For other symbols see text.

Fig. 4.—Pulmonary vascular dilution curve in a patient with aortic stenosis and congestive heart failure.

In the majority of patients isotope dilution curves were obtained with the detector placed over both lung fields; in the patients without shunts and in those whose left-to-right shunts entered the right atrium or right ventricle, the two curves had essentially identical contours and the values of  $C_2/C_1$  agreed closely (Fig. 6). However, in 2 of the 4 patients with patent ductus arteriosus  $C_2/C_1$  calculated from the curve obtained from the left upper lung field exceeded the value from the curve recorded from the right upper lung field by 12 per cent and 14 per cent respectively (Fig. 7). In the patient with tetralogy of Fallot in whom a right subclavian-right pulmonary artery anastomosis had been performed the ratio over the right lung was 21 per cent greater than that over the left lung (Fig. 8).

When the isotope was injected into an antecubital vein, the ascending limb of the dilution curve generally exhibited an early peak prior to the main curve (Fig. 7). This was presumably an artefact and resulted from detection of the isotope passing through the axillary vein and superior vena cava prior to its arrival in the pulmonary circulation. It was possible to eliminate this artefact by injecting the isotope into a femoral or saphenous vein (Fig. 8).

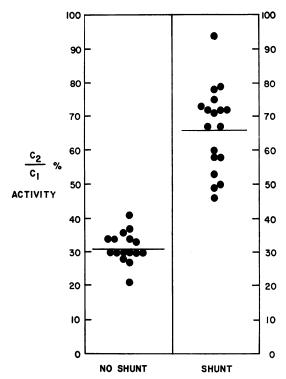


Fig. 5.—Results of the analysis of pulmonary vascular dilution curves in patients with and without shunts.

#### DISCUSSION

Indicator-dilution curves obtained by injecting dye into a peripheral vein and sampling from the pulmonary artery constitute an effective means of determining the presence or absence of left-to-right shunts (Braunwald et al., 1959). The method described in the present investigation is entirely analogous except that cardiac catheterization is avoided and the indicator circulating in the entire vascular bed beneath the scintillation crystal (arterial, capillary and venous) is detected.

The advantages of an accurate technique for the detection of left-to-right shunts without cardiac catheterization are apparent. The isotope method has been found to be useful in patients following an operation for closure of a left-to-right shunt. It may be undesirable or unnecessary to carry out post-operative catheterizations on many such patients, but knowledge of the adequacy of the closure is certainly important. It is also frequently necessary to determine the patency of a Blalock-Taussig or other systemic-pulmonary anastomosis both in the early and the late postoperative periods, since disappearance of the continuous murmur does not necessarily indicate cessation of blood flow through the shunt. It may be difficult or even impossible to make this determination by cardiac catheterization since in patients in whom such an anastomosis has been carried out it may not be possible to pass the tip of the catheter into the pulmonary artery. The recording of pulmonary vascular dilution curves, however, affords a simple method for assessing the patency of the anastomosis.

Four patients in the present series had small left-to-right shunts with pulmonary to systemic flow ratios ranging from  $1 \cdot 1/1 \cdot 0$  to  $1 \cdot 2/1 \cdot 0$ , and in all of them the presence of the shunt could be detected by the isotope method. Thus, the technique appears to be both sensitive and accurate.

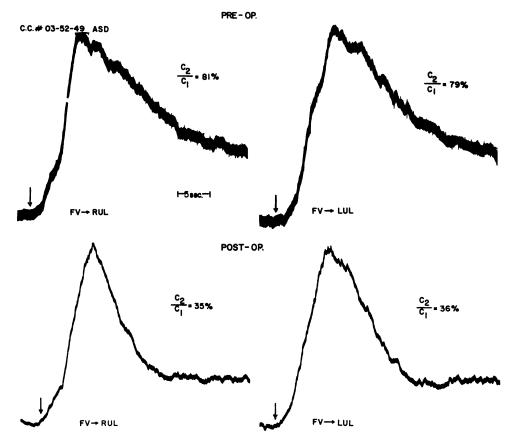


Fig. 6.—Pulmonary vascular dilution curves in a patient with an atrial septal defect prior to operation (top) and after complete closure (bottom). The curves on the left followed injection into a femoral vein (FV) with the detector placed over the right upper lung field (RUL). The curves on the right followed placement of the detector over the left upper lung (LUL). The curves over each lung field are similar but a marked fall in  $C_2/C_1$  occurred after closure of the defect.

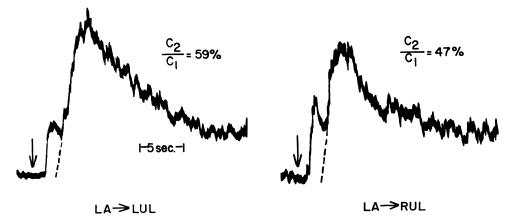


Fig. 7.—Pulmonary vascular dilution curves in a patient with patent ductus arteriosus. The curve on the left was obtained with injection into the left antecubital vein (LA) and the detector placed over the left upper lung field (LUL). The curve on the right was obtained with the detector over the right upper lung field (RUL).

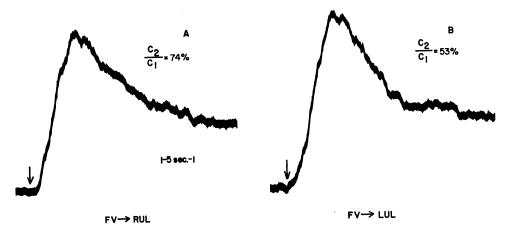


Fig. 8.—Pulmonary vascular dilution curves in a patient with tetralogy of Fallot following a right subclavian-pulmonary artery anastomosis. The curve on the left was obtained with femoral vein injection and the detector placed over the right upper lung field (RUL). The curve on the right was obtained with the detector over the left upper lung field. (LUL).

It can be employed as a convenient screening test in patients with heart murmurs of uncertain aetiology. If the curve indicates the presence of a shunt, right heart catheterization is necessary for localizing its site of entry into the heart, the magnitude of the shunt and the pressures in the chambers of the right side of the heart.

It is of interest that in two of the four patients with patent ductus arteriosus a significantly greater fraction of the isotope recirculated through the left lung than through the right. The recording of pulmonary vascular dilution curves from both upper lung fields could serve as a simple diagnostic test in patients with continuous murmurs. In those in whom the left-to-right shunt is into the main pulmonary artery or the right side of the heart, i.e. patients with aortico-pulmonary windows, ruptured aneurysms of the sinus of Valsalva, etc., the curves obtained over both lung fields may be expected to be identical. On the other hand, the curves will be dissimilar in some of the patients with patent ductus arteriosus in whom the shunt is into the left pulmonary artery. Study of a larger series of patients will, of course, be required to determine the ultimate value of the technique for this particular application.

Although præcordial isotope dilution curves have been successfully employed in determining the presence or absence of cardiac shunts, such curves usually do not detect shunts which enter the pulmonary artery. Furthermore, since præcordial placement of the crystal results in the detection of isotope in both sides of the heart, the shapes of the resultant curves are determined by a number of factors which do not influence the pulmonary vascular curves. The presence of regurgitation at any of the four valves tends to prolong the descending limbs of the præcordial curves, owing to slowed washout of isotope from the ventricles. Pulmonary vascular curves would not be greatly modified by mitral and/or aortic valvular regurgitation, although these curves could be influenced by tricuspid or pulmonary insufficiency. Thus, in our experience, placement of the detector over the lung fields rather than over the præcordium offers substantial advantages in the study of patients suspected of having left-to-right shunts.

## **SUMMARY**

A simple technique for the recording of indicator-dilution curves from the pulmonary vascular bed and its application to the detection of left-to-right circulatory shunts is described. A gamma-emitting isotope, I<sup>131</sup>-labelled diodrast, was injected intravenously and its activity in the pulmonary vascular bed determined with a scintillation detector placed over the upper lung field. In the 17

patients in whom the presence of left-to-right shunt was subsequently proved, the descending limb was selectively prolonged, and simple analysis of the curves in a total of 33 patients allowed determination of the presence or absence of a shunt. The advantages of placing the detector over the lung fields as compared to the præcordium are described. The clinical value of this simple technique in the study of patients following cardiac operations and in the screening of patients with heart murmurs of uncertain aetiology is discussed.

#### REFERENCES

Braunwald, E., Pfaff, W. W., Long, R. T. L., and Morrow, A. G. (1959). Circulation, 20, 875.

—, Goldblatt, A., Long, R. T. L., and Morrow, A. G. (1961). Brit. Heart J. (In Press).

Cornell, W. P., Braunwald, E., and Morrow, A. G. (1960). Med. Ann., Dist. of Columbia, 29, 67.

Cournand, A., Donato, L., Durand, J., Rochester, O. F., Parker, J. O., Harvey, R. M., and Lewis, M. L. (1960).

Trans. Assoc. Amer. Physic, 73, 283.

Dollery, C. T., West, J. B., Wilcken, D. E. L., Goodwin, J. F., and Hugh-Jones, P. (1961). Brit. Heart J. (In Press).

Dollery, C. T., West, J. B., Wilcken, D. E. L., Goodwin, J. F., and Hugh-Jones, P. (1961). Brit. Heart J. (1961). Greenspan, R. M., Lester, R. G., Marvin, J. F., and Amplatz, K. (1959). J. Amer. med. Ass., 169, 667. Huff, R. L., Parrish, D., and Crockett, W. (1957). Circulation Res., 5, 395. Lammerant, J., and de Visscher, N. (1956). Acta Cardiol., 11, 244. MacIntyre, W. J., Prichard, W. H., and Moir, T. W. (1958). Circulation, 18, 1139. Prinzmetal, M., Corday, E., Spritzler, R. V., and Flieg, W. (1949). J. Amer. med. Ass., 139, 617. Shapiro, W., and Sharpe, A. R. (1960). Amer. Heart J., 60, 607. Shipley, R. A. and Clark, R. F. (1956). Circulation Res. 4 456.

Shipley, R. A., and Clark, R. E. (1956). Circulation Res., 4, 456.

Turner, J. B., Salazar, E., and Gorlin, R. (1960). Amer. J. Cardiol., 6, 1004.

Veall, N., Pearson, J. D., Hauley, T., and Lowe, A. E. (1954) Proc. Second Radioisotope Conf., Oxford, July, 1951.

London, Butterworth Scientific Publication, p. 183.